

Facts and ideas from anywhere



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PRESIDENT CLINTON'S CHOLESTEROL NUMBERS

It has been reported that President Clinton's serum cholesterol numbers not long before his coronary bypass operation were the following (in mg/dL): total cholesterol, 210; low-density lipoprotein (LDL) cholesterol, 136; high-density lipoprotein cholesterol, 44; and triglycerides, 130. I suspect that most US physicians would not treat patients with such values, and

apparently Clinton had similar cholesterol values when he was totally asymptomatic. According to the guidelines (1988, 1993, 2001), patients with these numbers would not be treated with cholesterol-lowering drugs. A total cholesterol of 210 mg/dL is the average for adults in the USA, and Clinton's LDL cholesterol of 136 is only 6 mg/dL above the average for adults in the USA. If we are going to make a dent in atherosclerotic cardiovascular disease, we need to lower everyone's LDL cholesterol to <100 mg/dL, and it is much better to do that before an atherosclerotic event than afterwards. If every American reduced his or her LDL cholesterol by 50%, the health of this nation would skyrocket. The Heart Protection Study demonstrated that an LDL of 100 mg/dL is actually not low enough. To prevent plaques from forming in our arteries, the LDL probably has to be as low as 60 mg/dL. There is evidence that endothelial cell function is not normal until the LDL cholesterol is about 60 mg/dL.

HEALTH CARE COSTS OF OBESE VS NONOBESE INDIVIDUALS

Raebel and colleagues (1) from Denver, Colorado, and Tucson, Arizona, conducted a retrospective study of obese and nonobese individuals matched by age, sex, and medical clinic. A total of 539 obese and 1225 nonobese persons were examined. Obese patients had more hospitalizations, prescription drugs, professional claims, and outpatient visits. They also used more cardiovascular, intranasal, allergy, asthma, ulcer, diabetes mellitus, thyroid, and analgesic drugs. Total costs between groups were different: a median of \$585 for obese and \$333 for nonobese patients. Cost differences were primarily due to medications. Thus, over a 1-year period, health care costs for obese persons are higher than for nonobese persons, primarily because of prescription drugs. Our medical bills would decrease if we all lost some poundage.

BODY WEIGHT AND AIR TRAVEL

Americans gained an average of 10 pounds through the 1990s. Three physicians at the Centers for Disease Control and Preven-

tion calculated that to fly those extra pounds, airlines burned 350 million more gallons of fuel in 2000 at a cost of \$275 million (2). The extra fuel burned resulted in an additional 3.8 million tons of carbon dioxide emissions and other pollutants. The nation's airline carriers, of course, don't factor in how much passengers weigh when determining ticket prices.

PEDOMETERS

I wore a pedometer daily for years but recently lost it. In October 2004, *The Wall Street Journal* evaluated 6 pedometers and found that only 2 were reasonably accurate (3): Digi-Walker SW-200 and the New-Lifestyles NL-2000. These were the only models within 5% of the actual measured mileage. The Accusplit Alliance 1510, the Freestyle Pacer Pro, the Omron HJ 105, and the Oregon Scientific PE316CA were $\geq 25\%$ under or over the actual measured mileage. The website www.pedometers.com offers reviews of pedometers based on scientific research. *Consumer Reports* also lists its reviews on www.consumerreports.org.

MORE GUIDELINES FOR TREATMENT OF HYPERTENSION

The United Kingdom's National Institute for Clinical Excellence recently recommended combination drug treatment for adults with hypertension (4). Previously, it recommended that patients be given one antihypertensive drug; if that drug failed to control the blood pressure adequately, an antihypertensive drug from another class would be substituted. The guidelines now recommend a combination of antihypertensive drugs. Treatment should begin with a low-dose diuretic of the thiazide type; beta-blockers should be added as a second line of treatment, with a dihydropyridine calcium channel blocker added as a third line. In patients at high risk of new-onset diabetes mellitus, the second-line treatment should be an angiotensin-converting enzyme inhibitor, with a beta-blocker being added only as a fourth line. Intervention was recommended, however, only for people with blood pressures $\geq 160/100$ mm Hg. This group also recommended that patients with a cardiovascular risk of $\geq 20\%$ should be treated. These guidelines on hypertension are available at www.nice.org.uk. The United Kingdom is clearly behind the USA in trying to prevent strokes, aortic dissection, and chronic renal disease. I recommend the Joint National Commission VII's recommendations (5). Waiting for the blood pressure to reach $>160/100$ mm Hg before starting drug therapy is absurd. Goals in the USA now are certainly $<140/90$ and optimally $<130/85$ mm Hg.

DEMAGOGUERY

According to Charles Krauthammer (6), one of my favorite editorialists, at a rally in Newton, Iowa, in 2004, vice presiden-

tial nominee John Edwards said: "If we do the work that we can do in this country, the work that we will do when John Kerry is president, people like Christopher Reeve are going to walk, get up out of that wheelchair and walk again." On August 7, 2004, in his radio address to the nation, presidential nominee John Kerry began his address with the claim that the stem cell "ban" is standing in the way of an Alzheimer's cure. Harvard's Dr. Dennis Selkoe in a presentation to the President's Council on Bioethics recently discussed the newest and most promising approaches to solving the Alzheimer's mystery. According to Krauthammer, a paraplegic nonpracticing physician, Selkoe reported remarkable progress in biochemically clearing the "plaque" deposits in the brain that lead to Alzheimer's. The phrase "stem cells" never crossed his lips. George W. Bush is the first president to approve federal funding for stem cell research. Twenty-two lines of stem cells are now available, up from just one line 2 years ago. There are 3500 shipments of stem cells waiting for anybody who wants them. No, Bush has not banned stem cell research.

ASSISTED LIVING FACILITY VS CRUISE SHIP LIVING FOR THE ELDERLY

A piece in the *Journal of the American Geriatrics Society* has suggested that living on a cruise ship provides a better quality of life and is cost effective for elderly people who need help to live independently (7). Elderly people, of course, often choose assisted living facilities, nursing homes, 24-hour-a-day home caregivers, or family support. Living on a cruise ship might be a better choice. According to Lee Lindquist, people >65 years who enjoy travel and have good cognitive function but need some help in daily living are ideal candidates for care on a cruise ship. Both cruise ships and assisted living facilities offer single-room apartments with a private bathroom, a shower with easy access, some help, cable television, security services, and entertainment. Cruise ships, however, have superior health facilities, with at least 1 physician or nurse available 24 hours a day. They have defibrillators, equipment for dealing with medical emergencies, and the ability to give intravenous fluids and antibiotics. Assisted living facilities, in contrast, almost never have physicians on site and seldom have nurses available 24 hours a day. Cruise ships also have a higher ratio of employees to passengers than do assisted living facilities. In the USA, an assisted living facility costs about \$2360 a month, or nearly \$29,000 a year. Living on board a cruise ship for the entire year can cost just over \$33,000. The authors calculated that the long-term cost for a person to live on a cruise ship from the age of 80 until death would be just over \$230,000 compared with \$228,000 for an assisted living facility.

OUR OLDER FOLKS

About 12% of the US population is ≥ 65 years of age (8). When people reach age 65, they can expect to live another 18 years on average. In the USA today, only 13% of persons aged ≥ 65 have \$250,000 or more in savings and investments, excluding the value of their primary residence, to support their retirement. That amount would provide no more than \$15,000 annually. Save your money! As William Baldwin said: "If you were planning to retire at 50 with \$1 million in the bank, you should be in perfect health and comfortable in a trailer park in Arkansas" (9).

AN EXHIBITION AT THE HOLOCAUST MEMORIAL MUSEUM IN WASHINGTON, DC

Between 1939 and 1945, more than 200,000 "incurable" patients in Germany were murdered under strict medical supervision (10). Among them were at least 5000 children—disabled boys and girls who had been singled out for euthanasia in state hospitals by a panel of "expert" physicians. Early inspiration for the German eugenics movement may have come from the USA. By the early 1930s more than half of US states had voluntary sterilization laws, under which >16,000 operations had been performed. Chief Justice Oliver Wendell Holmes upheld the state laws in the Supreme Court, commenting that in some cases "3 generations of imbeciles are enough." Eugenacists in Germany in 1933 cited these programs in defense of the Law for the Prevention of Genetically Diseased Offspring. Within a decade, 500,000 Germans had been forcibly sterilized for conditions ranging from alcoholism to schizophrenia. By 1939, Adolf Hitler had ordered his deputies to commence Operation T-4, a plan to execute all those deemed genetically unfit and a drain on natural resources. The original note authorizing T-4 is on display in the exhibition called "Deadly Medicine" amid a chilling collection of photographs, film clips, and medical paraphernalia.

PERSONAL AND GOVERNMENTAL DEBT

The average household's personal debt in the USA now stands at \$84,454 (11). The average household's share of government debt including Medicare and Social Security is \$473,456. The US government is now \$53 trillion in debt, and baby boomers will begin to retire in just 4 years. Americans' obligation today as taxpayers is >5 times the \$9.5 trillion they owe on mortgages, car loans, credit cards, and other personal debt. Someday there will be a financial reckoning.

WHEN IS ONE SERIOUSLY RICH?

Paul Johnson said: "My idea of being rich—or at least of *feeling rich*—is to have no debts, mortgage or overdraft, and to be able to pay all bills by return post. This may seem a fairly modest ambition, but if everyone in the West were in this position our societies would indeed merit the term affluent, and the world would be a much happier place" (12).

MOTOR VEHICLE CRASHES AND ANIMALS

In 2000, an estimated 6.1 million crashes of light vehicles (passenger cars, sport utility vehicles, vans, and pickup trucks) on US roadways were reported to police (13). Of these reported crashes, 247,000 (4%) involved collisions with an animal on the roadway. Each year, an estimated 200 people die in crashes involving animals, i.e., deaths from direct collisions or from driving off the road to avoid an animal. During 2001 and 2002, an estimated 27,000 motor vehicle occupants per year were involved in crashes from encounters with animals (predominantly deer) and treated for nonfatal injuries in US hospital emergency departments, 6% of whom were hospitalized for their injuries. The highest injury rate (21 per 100,000 population) from such crashes occurred among persons aged 15 to 24 years.

Nationally, nonfatal injuries from collisions of motor vehicles and large animals account for <1% of approximately 3 million motor vehicle injuries treated annually in US emergency depart-

ments. However, in rural areas with large deer populations, these crashes, their associated occupant deaths and injuries, wildlife laws, and property damage are important concerns. In Wisconsin, for example, deer-related crashes accounted for nearly 16% of all statewide police-reported motor vehicle crashes in 2002.

The same behaviors recommended to help prevent crashes in general are relevant for motor vehicle–animal crashes. Driving within speed limits, staying alert, reducing distracted or drowsy driving, and eliminating alcohol-impaired driving should give drivers, particularly teenagers and younger adults, more time to react and avoid collisions. Of course, universal use of proper restraints, including safety belts, child safety seats, and booster seats, is useful.

COMING PHYSICIAN SHORTAGE

Richard Cooper of the Health Policy Institute of the Medical College of Wisconsin argues that physician shortages in the USA are emerging and that they will probably worsen over the next 2 decades (14). By 2020 or 2025, the deficit could be as great as 200,000 physicians, a 20% shortage. The USA is not alone in coping with inadequacies in physician supply. Similar problems exist in Canada, the United Kingdom, Australia, and New Zealand. Unlike the USA, however, these other countries are actively addressing the problem. Already in the USA, according to Dr. Cooper, the number of physicians is no longer keeping up with the population growth. The ability to fully serve the population is further compromised by the increasing complexity of the care that physicians provide and the decreasing time commitment that many physicians are willing to make.

SEX CONCORDANCE BETWEEN PATIENT AND PHYSICIAN

Fang and associates (15) from San Francisco, California, assessed the characteristics of >92,000 visits to office-based physicians in the USA from 1995 to 2000. Female physicians were more likely than male physicians to see female patients in the specialties of primary care (73% vs 56%), psychiatry (72% vs 54%), dermatology (67% vs 56%), and pediatrics (52% vs 46%). In primary care the differences increased over time such that by 2000, 80% of visits to female primary care physicians were from women compared with 56% for male primary care physicians. Female primary care physicians saw younger patients, reported longer visits, and performed more preventive services than did male primary care physicians when seeing female patients.

PHYSICIANS AND PHARMACEUTICAL COMPANIES

I try to have a relatively open door policy with representatives of various pharmaceutical companies. I do that because I learn about their agents from them, and as dean of the A. Webb Roberts Center for Continuing Medical Education I am often requesting support for one medical meeting or another. Interactions with physicians, as David Blumenthal has pointed out, represent a huge investment by the pharmaceutical industry in marketing (16). In 2002, the industry expended 33% of its revenues on “selling and administration.” The marketing expenditures of the drug industry in the USA have been estimated to be from \$12 billion to \$15 billion yearly, or \$8000 to \$15,000 per physician. In 2001, the industry’s sales force of drug detailers, whose job is to meet individually with physicians and promote company

products, numbered nearly 90,000 in the USA—1 sales person for every 4.7 office-based physicians.

A common way in which the pharmaceutical industry interacts with practicing physicians is continuing medical education. By 2003 pharmaceutical companies were spending nearly a billion dollars annually on continuing medical education in the USA. The pharmaceutical industry also maintains relationships with the organizations to which physicians belong and for which they work. Drug companies are frequent financial sponsors of the annual meetings of physician organizations, and they also support those organizations’ special projects. Indeed, without that support many of these organizations would not exist.

Many physicians believe that their interactions with drug companies have educational value for themselves and also provide benefits for their patients, both because physicians are kept informed of available therapeutic agents and because the free samples they are given can be distributed to patients. Physicians also tend to be confident that they are invulnerable to any bias inherent in the educational content offered or supported by drug companies. Indeed, most residents and faculty members surveyed at a US medical school viewed a wide variety of interactions between drug companies and physicians as ethically acceptable. Despite the confidence of physicians in their ability to resist efforts by drug companies to affect their behavior, a substantial body of theoretical and empirical reports suggests that many physicians may be mistaken. When a gift or gesture of any size is bestowed, it imposes on the recipient a sense of indebtedness. The obligation to reciprocate, whether or not the recipient is conscious of it, tends to influence behavior.

It appears that physicians, organizations, drug companies, and the government have become relatively uncomfortable in recent years with the nature, extent, and consequences of interactions between physicians and pharmaceutical companies. Professional, industry, and government groups have attempted to clarify standards that differentiate appropriate from inappropriate relationships and therefore to reduce the frequency of suspect interactions. These relatively new guidelines and regulations seem to embrace the view that some relationships between drug companies and physicians are ethically appropriate, beneficial, and unavoidable and that the challenge is to contain those relationships within acceptable boundaries and to avoid certain egregious practices. Most physicians view as appropriate the provision by drug companies of modest gifts, free drug samples, support for educational programs, and a number of other services for physicians. Physicians are less likely, however, to view as acceptable the receipt of gifts and services that are either very valuable or unrelated to a professional purpose. The ultimate arbiter of the nature, extent, and consequences of interactions between drug companies and physicians is the medical profession itself.

SHE WRITES MORE THAN MOST READ

In just over 2 decades, 54-year-old novelist Nora Roberts has written 157 books (7.9 million words), and 116 of them were best sellers (17). She writes 3 paperbacks and 3 hardbound books a year. That’s 300,000 words, probably more than most Americans read. Ms. Roberts was born Eleanor Marie Robertson. She grew up in an Irish-American family in Silver Spring, Maryland, just outside of Washington, DC, with 4 older brothers. After graduat-

ing from a parochial high school, she skipped college, married at 17, and moved to western Maryland. She initially had a job as a legal secretary but soon got pregnant and stayed home. During a blizzard in 1979, after an endless round of games with her 2 small sons, she wrote a romance book called *Melodies of Love*. She was unable to find a publisher for it or for the next 5 books she wrote. That changed in 1981 when romance publisher Silhouette accepted *Irish Thoroughbred*, the story of a girl from the Emerald Isle who came to Maryland and met a nice, studly American horse-farm owner. After a few intimate escapades they wed. She has continued that formula: girl meets manly but sensitive boy; they have explosive physical adventures together and find real fulfillment in marriage. She and her first husband split up in 1983 and thereafter she started writing more or less every weekday from 8:00 AM to 4:00 PM. Two years later she married the carpenter who came to build her bookcases, and they have been happy ever since. She now grosses \$60 million a year and owns the copyright to all of her books. (J. K. Rowling, author of the Harry Potter series, earns \$147 million per annum.) According to *Forbes*, \$1.4 billion was spent in 2003 on romance novels, 2093 new titles of romance fiction appeared that year, 34% of all popular fiction sales were romance tales, and nearly 50% were bought by women aged 25 to 44. Medical writing does not pay quite as well as romance writing.

US WAR DEATHS

So far in the Iraqi war, >1200 US soldiers have died and >8000 have been injured. Some of the injuries were so bad that death probably would have been better. The numbers of US soldiers dying in our wars are shown in the *Table* (18). The number of deaths in the Iraqi war would be far greater if medical care today wasn't so superb. The USA now spends 7 times more on war than on education.

Table. Major wars involving the USA: numbers of service personnel dying and wounded*

Conflict	Deaths		Wounded but survived
	Combat	Other†	
Revolutionary War (1775–1783)	4435	—	6188
War of 1812 (1812–1815)	2260	—	4505
Mexican War (1846–1848)	1733	11,550	4152
Civil War (1861–1865)			
Union	110,070	249,458	275,175
Confederate	74,524	124,000	137,000
Combined	184,594	373,458	412,175
Spanish-American War (1898)	385	2061	1662
World War I (1917–1918)	53,513	63,195	204,002
World War II (1941–1945)	292,131	115,185	607,846
Korean War (1950–1953)	33,651	—	103,284
Vietnam War (1964–1972)	47,369	10,799	153,303
Gulf War (1990–1991)	148	145	467
Iraqi War (2003–)	>1200		>8000

*Source: www.rationalrevolution.net (18).

†Deaths from disease, privation, and accidents, including losses among prisoners of war.

IGNAC SEMMELWEIS AND CHILDBED FEVER

Sherwin B. Nuland, MD, the author of *How We Die* and *Lost in America*, among other books, has now written *The Doctors' Plague*, a story of Ignac Semmelweis (1818–1865) and his discovery of the cause of childbed fever (19). Semmelweis was the fourth son of a successful Jewish grocer. His schooling in both Hungarian and German left him with a hatred of writing. He began studying law but quickly switched to medicine, completing his degree in 1844 and becoming accredited in midwifery the same year. At that time, Vienna's Allgemeine Krankenhaus was the world's largest and most famous hospital. It housed 2 obstetrical clinics, the first for teaching medical students and the second for training midwives. By 1846 Semmelweis had been appointed assistant to the director of the First Obstetrical Clinic. At the time of his appointment, childbed fever killed 1 in 6 women in labor admitted to Vienna's hospitals. No one knew the cause. A commonly believed theory blamed noxious airs. A result was much drilling of holes through the hospital walls and doors in an attempt to improve ventilation.

Semmelweis quickly noticed that the women's mortality rate in the clinic for medical students was 3 times that in the clinic for midwives! Between 1841 and 1846, he calculated that 1989 women had died in the company of medical students out of 20,042 admissions, or 10%. The comparable figures for midwives were 691 deaths out of 17,791 hospital confinements, or 3%. Women entering the Allgemeine Krankenhaus were well aware of these differences. Those admitted to the first clinic often begged to be admitted to the second (midwife) clinic. Giving birth on the streets of Vienna was safer than within the walls of the city's most prestigious hospital.

Semmelweis correlated the soaring incidence of childbed fever with the introduction of autopsies into the hospital during the 1820s. When his friend Jakob Kolletschka, a professor of forensic medicine, died of a disease indistinguishable from that of women with fatal puerperal fever, Semmelweis became convinced that somehow cleanliness was at the root of the problem. Kolletschka had cut himself with a knife while conducting an autopsy. Semmelweis suggested that particles from the cadaver must have been transferred into Kolletschka's bloodstream, therefore causing his death. Medical students were exposed to the same particles from cadavers while performing autopsies. The students could have been a source of the disease that soon overtook the women they went on to care for.

Semmelweis tested his idea by introducing new rules for hygiene in May 1847. He required physicians and students to wash their hands with soap and warm water, to scrub their nails, and to rinse their hands with a chlorine solution until they were slippery. By June, death rates had plummeted. They fell still further when Semmelweis realized that transmission of particles from cadavers could take place from one woman to another. He could stop the fever as it moved through a ward by simply insisting on chlorine disinfection of a doctor's hands after the examination of each woman. He concluded that it was the physicians and their medical students who had caused an entirely unnecessary epidemic of deaths. The uterus after birth had to be seen as a huge fresh wound. Only obsessive hygiene could prevent it from becoming a portal for fatal particles introduced through contaminated vaginal examinations.

His results were striking and convincing. But Semmelweis, for unclear reasons, did not publish his findings. Instead, he left it to colleagues and friends to circulate his discovery, and that was done in a local medical journal in December 1847, in April 1848, and in November 1848.

Semmelweis also angered his conservative medical colleagues—and especially his boss, Johann Klein, who was head of the Department of Obstetrics and Gynecology—by his relative revolutionary zeal against the rights of kings and emperors. Klein rejected Semmelweis' arguments concerning cleanliness, as did his colleagues. He probably felt angry that this precocious Hungarian was making orthodox practices and practitioners look not only ridiculous but also dangerous. It was Klein, incidentally, who had insisted that medical students examine cadavers in the first place, and it was he who had relaxed constraints on conducting vaginal examinations during labor. Semmelweis seemed to be saying that Klein's policies were the direct cause of the epidemic.

When Semmelweis' temporary appointment came up for renewal in March 1849, Klein blocked his application, despite appeals from senior medical colleagues, such as the celebrated pathologist Karl von Rokitansky, who eventually performed 31,000 autopsies at that hospital, and the skilled diagnostician, Josef Skoda. Semmelweis was even unable to establish himself as an independent physician with the right to admit patients to the hospital. Hurt and insulted, he left Vienna for Pest, Hungary, without even telling his friends or supporters. Although his parents in Pest were now dead, his sister and brother, a Catholic priest who had converted from Judaism, were still living there.

The academic standards at the University of Pest were low. In May 1851, he was given an unpaid position in the obstetric division of St. Rochus Hospital, where he once again introduced chlorine disinfection with again dramatically successful results. His work earned him the chair in theoretical and practical midwifery in 1855, when he was 37. He married the 21-year-old Maria Wiedenhofer and, in 1858, published his first paper describing his work in a Hungarian medical journal.

But again, he aroused conflict. Opposition to his work grew stronger. Even the great pathologist Rudolf Virchow denounced him. About the same time, however, Semmelweis began writing the book that would finally destroy as well as make his reputation. *The Etiology, Concept, and the Prophylaxis of Childbed Fever* was published in 1861, the year the Civil War started in the USA. It is divided into 2 parts. In the first, Semmelweis assembled a vast collection of data, presented in 63 detailed tables, to construct a theory for the transmission of puerperal fever. In addition to his observations among women, he included results from experiments on rabbits, which lent support to his view that particles derived from autopsies provided the source of disease. The second part attacked his critics. This was the part that got him into serious trouble. Many leaders in obstetrics in Europe were vilified.

While the book collected all of Semmelweis' investigations into one volume for the first time, it met with harsh reviews and had little impact in preventing the dreaded puerperal fever. Probably as a consequence, Semmelweis' mental state deteriorated. He roamed the streets of Budapest muttering to himself and distributing pamphlets directed against those who refused to follow his teachings. He seemed to swing from periods of excitement and energy to periods of paralyzed depression. By July 1865, he

was clearly deranged. On July 28, his wife had him committed to psychiatric care. Incarceration in a brutal asylum would be a more accurate description. He died on August 13, at age 47.

The long-held view was that Semmelweis died from a bacterial infection of the blood sustained after a cut to his finger. But the excavation of his remains in 1963 and the discovery of new documents in the 1970s suggest a more tragic end. It seems that Semmelweis was lured to the Viennese asylum by his wife. He thought he was traveling first to a spa and then to Vienna to visit and work in the house of a longtime friend and advocate. Once he had arrived, 3 doctors, none of whom was a psychiatrist, approved his involuntary imprisonment in one of Vienna's nastier institutions. He resisted efforts to constrain him, after which he was put into a straightjacket and locked in a darkened cell, where he was beaten for his recalcitrance. When he died shortly thereafter, the medical press simply noted his death, and there were no obituaries recognizing his accomplishments. His wife, Maria, did not attend his funeral.

For whatever reason, Semmelweis was unable to match his magnificent discovery with an ability to persuade his colleagues of their part in causing puerperal fever. This personal failure, however, does not detract from the obsessive tenacity with which he pursued his cause.

NURSE-MIDWIVES IN THE USA

According to Mona T. Lydon-Rochelle, PhD (20), recent US statistics show an ever-increasing use of intrapartum interventions such as induction of labor (in 21% of deliveries) and cesarean delivery (26%) and of perinatal outcomes such as preterm delivery (12%) and low birth weight (8%). Dr. Lydon-Rochelle believes that if maternity care in the USA is to improve, the input and collaboration of professionals in midwifery, medicine, public health, and public policy will be required. In most European countries, midwives deliver most infants, and perinatal health outcomes apparently are good. Midwives in Ireland, Scotland, and England deliver >65% of all babies, and the proportions in Denmark, Sweden, Norway, Finland, and Germany exceed 85%. These countries have fewer obstetrical interventions, lower maternal, neonatal, and infant mortality rates, and higher rates of breastfeeding than the USA.

The first nurse-midwives in the USA were members of a pioneer profession that served the poor. The most important period of development in nurse-midwifery began in the 1920s, when, to address high maternal and infant mortality, they provided maternity care in areas that lacked it. The Frontier Nursing Service initiated the first nurse-midwifery program in the USA. British-trained midwives were recruited to rural Kentucky to "safeguard the lives and health of mothers and children." Their care resulted in marked reductions in maternal and infant mortality. In 1932, the Maternity Center Association opened in Harlem, the first educational program for nurse-midwives in the USA. By 1944, six schools were educating nurse-midwives.

Training for nurse-midwifery is rigorous. Nurse-midwives are educated in both nursing and midwifery and graduate from a program accredited by the American College of Nurse-Midwives. To practice, they must pass an examination for certification by a national board. Today, 42 graduate educational programs, a number of them at prestigious medical institutions, offer master's

degrees in public health, science, and nursing, as well as doctoral degrees. Education focuses on the management of women's health care, particularly pregnancy, childbirth, the postpartum period, care of the newborn, and gynecology. The training promotes a noninterventional, individualized approach to normal pregnancy and childbirth, involving a certain amount of education of women—an approach that is often time consuming.

Today, approximately 6200 nurse-midwives are in clinical practice nationwide in the USA, a relatively small number compared with the 45,000 board-certified obstetrician-gynecologists, 17,000 family practice physicians, and other physicians who attend the nearly 4 million births each year in the USA. Despite their relatively small numbers, however, nurse-midwives attended 10% of live births involving vaginal delivery in the USA in 2001, a marked increase from <5% in 1989. The women served by nurse-midwives are known to have relatively low rates of obstetrical interventions and procedures, such as induction of labor, episiotomy, the use of epidural anesthesia, and cesarean delivery. They also report high levels of satisfaction, and the models of care used by nurse-midwives have been shown to be cost effective. Nearly half of nurse-midwives are employed by physician practices and hospitals. In nearly all states nurse-midwives have prescription-writing authority. Medicaid reimbursement for the services they provide is mandatory in all states, 33 of which also require reimbursement by private insurance companies.

JOHN SNOW, CHOLERA, AND THE PUMP HANDLE IN LONDON

On August 31, 1854, London experienced an epidemic of cholera (21). John Snow, MD (1813–1858), a legendary figure in epidemiology, suspected water from the Broad Street pump as the source of disease. To test his theory, Snow reviewed death records of area residents who died from cholera and interviewed household members, documenting that most who had died had lived near and had drunk water from the pump. Snow presented his findings to community leaders, and the pump handle was removed on September 8, 1854. Removal of the handle prevented additional cholera deaths, supporting Snow's theory that cholera was a waterborne contagious disease. Despite the success of this investigation, the cause of cholera remained a matter of debate until *Vibrio cholerae* was isolated in 1883. Snow's studies and the removal of the pump handle became a model for modern epidemiology.

JOSEPH GOLDBERGER, PELLAGRA, NIACIN, AND ATHEROSCLEROSIS

In 1913, my father, Stewart Ralph Roberts, MD (1878–1941), wrote a book called *Pellagra: History, Distribution, Diagnosis, Prognosis, Treatment, Etiology* (22). Among its 272 pages (excluding the index), 34 discussed the cause of pellagra, focusing mainly on the corn and infectious theories. He had spent several months in 1912 in Italy, where pellagra was endemic. On the next to the last page of my father's book, he wrote: "At the present time further discussion on the cause of the disease (pellagra) is to no purpose. If we knew the cause, it could probably be stated in a sentence—certainly in a page. Pellagra is either an infection or an intoxication—it cannot be both. It cannot be caused by the poisons of both corn and protozoa." And his last sentence in the book was "In the language of a European physician, 'Pellagra has

appeared in America, and no doubt in America the true cause of the disease will be discovered.'"

In February 1914, Surgeon General Rupert Blue asked Dr. Joseph Goldberger (1874–1929), a surgeon in the Public Health Service in Washington, DC, stationed at the Hygienic Laboratory, the precursor of the National Institutes of Health, to take over the pellagra studies from Claude Lavinder, who had requested reassignment. Goldberger's career thereafter and before has been beautifully recorded by Alan M. Kraut in *Goldberger's War. The Life and Work of a Public Health Crusader* (23). Goldberger's early life had attuned him to the poverty he would see in the South, where most of the pellagra cases were concentrated. His early career experience fighting yellow fever in Mexico had prepared him to recognize the epidemiological connections between poverty and particular diseases.

Joseph Goldberger emigrated with his parents and 5 siblings from Giralt, Hungary, to the USA in 1883, when he was 9 years of age. His father, Samuel, a former shepherd, peddled until he accumulated sufficient capital to open his grocery store on the Lower East Side neighborhood of Manhattan. The streets surrounding the grocery store were dirty and littered with trash and animal waste. The overcrowded living and working conditions in the immigrant quarter made newcomers vulnerable to tuberculosis, the great killer of the 19th century, as well as to a plethora of ailments and injuries.

Like millions of other immigrant families, the Goldbergers saw education as the port of entry to American life. At age 16, Joseph Goldberger graduated from high school and entered the College of the City of New York, where he initially studied engineering but soon switched to medicine. After the second year, he enrolled in the Bellevue Hospital Medical College, where he graduated in 1895 at age 20. He scored highest among his classmates on the college's examinations. After completing his 2-year internship at Bellevue Hospital, he set up an office in his parents' new East 72nd Street apartment to practice. After 3 months and only \$17.15 in income, he moved to Wilkes Barre, Pennsylvania, where he was more successful in private practice, but he didn't particularly enjoy it. In June 1898, during the Spanish-American War, he tried to join the US Navy but was turned down; he then applied and was accepted into the US Marine Hospital Service (which in 1912 became the US Public Health Service). From 1899 until 1914, Joseph Goldberger battled yellow fever in Mexico, Puerto Rico, Mississippi, and Louisiana; typhoid fever in Washington, DC; dengue fever in Texas (Brownsville); typhus in Mexico City; measles in New York City; and diphtheria in Detroit. Goldberger contracted 3 of the diseases he was studying: yellow fever, dengue fever, and typhus.

When he was assigned to supervise the federal government's pellagra investigation, 40-year-old Goldberger, newly promoted to the rank of surgeon, spent time in the Hygienic Laboratory's library learning all he could about pellagra. He knew that it was characterized by a symmetric photosensitive red rash, which in older individuals was often dry and scaly; acute diarrhea; and mental aberrations (the 4 D's: dermatitis, diarrhea, dementia, and death). The disease was rampant, particularly in the South. In 1912, South Carolina had 30,000 cases, with a mortality rate of 40%.

One report that attracted his attention discussed the diet at Illinois insane asylums. Goldberger noted, "Meat was given only

twice a week and the general diet was deficient in proteins." Some physicians in Europe at the time believed that pellagra was caused by eating only maize (corn). When pellagra was rampant in Italy, Italians apparently ate practically no meat, fish, milk, or eggs. The Illinois report, despite its focus on diet, concluded (like most physicians at the time) that pellagra was most likely due to an infection. Goldberger was already aware that certain foods prevented illnesses, such as scurvy's being prevented by eating citrus fruit and beriberi's being successfully treated with extract from rice bran. Thus, heading south in March 1914, Goldberger believed inadequate diet to be the cause of pellagra.

His first stop was Staunton, Virginia, where he visited the Western State Hospital, one of Virginia's several insane asylums. In the following months Goldberger visited asylums, orphanages, and prisons, places where pellagra frequently appeared, in Georgia, Alabama, Florida, Kentucky, South Carolina, Louisiana, and Mississippi. Everywhere he went he asked the institution's superintendents for data on pellagra incidence, diets of inmates and staff, especially corn consumption, and permission to inspect their sanitary conditions. As he had done in the alleys of Mexico, Puerto Rico, and Texas, he hunted for insects that might be carrying the disease to victims. What struck Goldberger most was that in all the institutions he visited, not a single staff member had pellagra. He believed that no infectious disease selected victims by status.

On June 26, 1914, Goldberger for the first time told the public health community what he thought about pellagra. In an article titled "The Etiology of Pellagra," he drew on what he had learned in his readings and initial travels. He believed the following: 1) that pellagra was triggered by a flawed diet and was not an infectious disease; 2) that pellagra was a disease dependent on a still-unknown fault in the diet in which the animal or leguminous protein component was disproportionately small and the nonleguminous vegetable component was disproportionately high; 3) that pellagra did not develop in those eating a well-balanced diet; and 4) that pellagra was generally seen in rural areas where poverty was rampant. He believed that residents of very poor cities had a more varied diet than the poor in rural sections. Goldberger urged improving the pellagrins' diet.

Goldberger began his feeding experiments at the Methodist Orphan's Home in Mississippi in September 1914. He also did experiments at the Baptist Orphanage. He hoped that he would cure sick children and that his success would persuade physicians that his dietary hypothesis was correct. From the very beginning, Goldberger recommended for pellagrins an abundance of fresh milk, eggs, fresh lean meat, beans, and peas "fresh or dried, not canned." Early on, he believed that beans and peas would provide the ingredients to prevent and to cure pellagra, but that later proved incorrect. Milk was described as "the most valuable single food." He urged adults to drink 1½ to 2 pints a day. He recommended 4 eggs per day and encouraged adults to take "at least a half pound of lean meat a day." Although Goldberger and his colleagues did not subscribe to the corn theory of pellagra, he recommended excluding corn. He also recommended reducing the amount of other "carbohydraceous articles, such as the newest cereal breakfast foods, molasses, jams, or starch." Once the pellagra symptoms disappeared, corn consumption could be resumed as long as the diet continued to include "an abundance of milk, meat, or legumes." Diet and rest were all that were prescribed.

His experiments in the Mississippi orphanage were beginning to pay off. Beginning in mid-September 1914, the diets at both orphanages were "supplemented by the Public Health Service." At the Methodist Orphan's Home, 67 of the 79 victims spent the anniversary of their pellagra episodes under the observation of Goldberger, and none showed signs of a recurrence. At the Baptist Orphanage, 105 of 130 patients completed the anniversary of their attack under observation, and only one had a recurrence. The news was also positive from the Georgia State Sanitarium at Milledgeville, where adult inmates were similarly tested. The same dietary changes made in the orphanages were made in the asylum's 2 wards. None of the group of 72 patients had presented recognizable evidence of recurrence of pellagra after going on the new diet. In comparison, at an orphanage without dietary intervention, recurrences occurred the following year among 18 of 31 children with pellagra (58%) in 1912, 16 of 21 (76%) in 1913, and 56 of 75 (75%) in 1914.

Although Goldberger was convinced that pellagra was due to a missing "fault" in food, to be more convincing he needed to induce the disease in healthy individuals by changing only their eating habits. He tried this at the Rankin State Prison Farm in Mississippi. Goldberger dangled the promise of pardons before approximately 80 inmates. All the prisoners had to do was volunteer to spend the next 6 months eating the traditional southern diet. Both the governor and Goldberger were candid as to the risks. Five months after the pellagra-inducing diet was started, 6 of the 11 who remained in the study had developed symptoms justifying a diagnosis of pellagra. Newspapers all over the country trumpeted Goldberger's demonstration that he could induce pellagra. Although Goldberger could not identify the pellagra preventive, he knew what kinds of foods contained it and what the dire results were when it was absent. The 11 prison volunteers were considered heroes and received pardons.

Predictions of the demise of the germ theory of pellagra were premature. Although by 1916 Goldberger had convinced himself and an increasing number of physicians that pellagra was triggered by a dietary deficiency, he had not convinced enough peers to radically change the treatment of the disease throughout the USA. Pellagrins were still dying by the thousands. Goldberger decided to provide a dramatic demonstration. He exposed 16 volunteers—including his wife, Mary—to blood, nasal pharyngeal secretions, epidermal scales from pellagrous lesions, urine, and feces from patients with pellagra. Some volunteers experienced lymph node swelling and other forms of moderate discomfort, but none developed pellagra. Goldberger concluded that these experiments furnished no support for the view that pellagra is a communicable disease and strengthened the conclusion that pellagra is a disease brought about by a faulty diet.

On November 16, 1916, Goldberger presented his findings to the Southern Medical Association in Atlanta. (Surely Dr. Stewart R. Roberts, who practiced in Atlanta, was among those in attendance.) Despite the new evidence, many at the meeting continued to believe in a pellagra germ. Accepting pellagra as a disease without pathogen was still more than most could do, no matter how much they respected Goldberger.

Having studied institutionalized pellagrins, Goldberger turned to studying the general population, focusing on mill villages because of their high prevalence of pellagra. The mill village study

began in April 1916 and continued for 2½ years. Goldberger recruited George Wheeler, a physician who visited each village and household to determine the incidence of pellagra and the composition of the diet; Ralph Tarbett, a sanitary engineer who surveyed sanitary conditions; and Edgar Sydenstricker, brother of the novelist Pearl S. Buck and the chief statistician of the Public Health Service, who analyzed the data. Another squad gathered information on family income and food accessibility.

Goldberger's team collected data on 4399 individuals, among whom there were 115 definite and 73 suspected cases of pellagra, rates of 26 and 43 per 1000, respectively. Children ≤2 years old rarely had the disease. Boys and girls had a similar incidence up to age 20. After age 20, the disease was more prevalent in women than in men. Between ages 30 and 44, the incidence for men was 9 per 1000 and for women, 54 per 1000.

Pellagra incidence was unrelated to mill work (the rate among non-mill-working women was 4 times as high as that of mill-working women), pollution of a village's water supply, the incidence of typhoid (caused by fecal contamination), and the presence of insects. The most potent factors influencing the incidence of pellagra in the communities studied were low family income and "unfavorable conditions regarding the availability of food supplies." State health departments objected to Goldberger's recommendation that the government provide milk, eggs, and fresh foods to those in the South likely to develop pellagra. Discouraged, Goldberger returned in 1921 to his bench at the Hygienic Laboratory in Washington, DC.

After 1920, Goldberger tried to discover the essential dietary factor in pellagra by testing the preventive power of certain vitamin-rich foods (butter and cod liver oil, for example) and a vitamin-free protein (casein). He prepared pure proteins and conducted experiments in rats and dogs. After finding which foods prevented black tongue disease in dogs, he gave these foods to patients in Milledgeville. Dried brewer's yeast cured pellagra in the patients. Goldberger began to refer to brewer's yeast as possessing the pellagra-preventive (P-P) factor. Goldberger did not know why brewer's yeast cured and prevented pellagra, but it did and was inexpensive.

Without knowing it, Goldberger had stumbled onto a complex biochemical relation. The amino acid tryptophan and the vitamin niacin are related, but that relation was not fully understood until the 1930s. Tryptophan, not produced in the human body, is a precursor in the pathway to niacin. Niacin prevented pellagra. Goldberger understood none of these relations. He had learned earlier that tryptophan mixed in the foods in the Milledgeville patients cured pellagra, and now he was aware that brewer's yeast had the same effect.

With the human experiments, Goldberger and colleagues also learned that wheat germ and salmon were pellagra preventives. Wheat germ could be added to flour for those living in areas affected by pellagra, and canned salmon was both available to and affordable by southerners. When a terrible flood occurred in the Mississippi River bed in 1927, Goldberger urged the flood victims to include a baker's yeast preparation named Begex, canned salmon, and canned tomatoes in their diet as pellagra preventives. The Red Cross distributed 12,000 pounds of brewer's yeast in the flood-ravaged areas. It worked. Most pellagrins were cured in 6 to 10 weeks. The cost of prevention was 3¢ per day per person.

Goldberger did not live to see his P-P factor identified. As he delivered his last speech, a malignant tumor was growing in his body. An autopsy showed a hypernephroma; the renal carcinoma had not been detected during life. By the time of his death, Goldberger had become a public hero. His colleagues had nominated him for 5 Nobel Prizes, but he did not receive that honor. A bill was passed in both houses of Congress to give his widow, Mary Goldberger, a life pension of \$125 per month. The pension was gratifying but hardly sufficient. Other private donors came forth to help support his family.

The final piece of the pellagra puzzle came in 1937 when researchers at the University of Wisconsin identified nicotinic acid as the P-P factor in rats and dogs. Tom Spies (25) at the University of Cincinnati College of Medicine demonstrated that niacin cured human beings of pellagra and prevented the disease. Now, there was no doubt that the poor, even those with limited access to milk, fresh meat, eggs, and green vegetables, could be protected.

Another piece of the puzzle slipped into place in 1945. Biochemists at the University of Wisconsin demonstrated that those who blamed corn consumption for pellagra were not as clueless as Goldberger had asserted. Corn consumption depressed the level of nicotinic acid retained in the body. Eventually, it was learned that both human beings and animals have the ability to convert tryptophan into nicotinic acid under certain conditions. Pellagra was thus a deficiency of both tryptophan and nicotinic acid. Goldberger had come to the very periphery of the biochemical identity of the P-P factor. He did not know that other B vitamins, pyridoxine and riboflavin, are involved in the metabolism of tryptophan or that pyridoxine is required to synthesize niacin from tryptophan.

I have never seen a case of pellagra, and I doubt if many other practicing physicians have either. The only downside to preventing pellagra was the increased consumption of milk, meat, and butter. It's better to take a multivitamin, which generally contains about 40 mg of niacin, and forgo the milk and meat.

My father, Stewart Ralph Roberts, in a 1928 piece entitled "Pellagra of Today" wrote:

The majority of workers incline to the belief that it [pellagra] is a deficiency disease, probably involving 2 factors, proteins and their aminoacids and a vitamin deficiency factor, which Goldberger calls "pellagra-preventive"—P.P. Most of us seem to know the cause of pellagra until we really face it, and then it becomes vague and very distant, and we hazily conclude that the cause is over in the cupboard somewhere among the proteins and vitamins that are not there. At any rate, in the light of present-day knowledge, the work of Goldberger and his associates is an epoch in the study of the etiology and is the first thoroughgoing, well planned, persistently-pursued research that has aimed at the discovery of the food factors involved in terms of modern diet and nutrition. While the work so far done may not seem to explain all the facts and does leave others in the balance, it must remain a first epoch in etiology until a second disproving epoch occurs, should it ever occur (26).

DALE PASCHAL JONES

Dale Jones, 68, died on November 6, 2004, of complications of a head injury. The former president of Halliburton Corporation was also a loved member of the Baylor Health Care System Board of Trustees, where he served as chairman from 1998 to 2000. Dale Jones taught me something about note writing, and

HALLIBURTON COMPANY

STERLING PLAZA, STE 1225
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Dale Jones

July 21, 2000

Dear Bill,

You sure know how to ask the right questions; maybe that comes through medical school. What can interesting and thought-provoking interviews you did with Dr. R.V. Lee! He is a unique person, and it was good to get to know him through your interview.

The history of dermatology presented by Dr. Menter was helpful to a relative newcomer like me.

And your "Facts and Ideas from Anywhere" always contains educational items. Thanks for the diet comments, the expiration of medicine, and the saving money tip. I just may begin an annual check delivery to my grandchildren.

We value your contribution at BUMC and Baylor Health Care System.

Sincerely,
Dale Jones

10/6/04

Dr. Roberts -

You're droo't again! What a delightful article you prepared on Dr. Boland, and what an asset he is to BUMC! Thank you very much.

As chair of the BHS advisory committee on Clinical Transformation, I read with great interest the CT article and the baseline medication studies article in the July BUMC Proceedings. And the medication article in the October issue was also very enlightening. Thank you for highlighting these issues, and I hope you will continue to do so in coming issues.

As you know, the CT project cannot be successful unless we have active support and leadership from BHS physicians. I think you, personally, can do a lot to bring physicians along in their understanding of the need for change in order to have significantly improved outcomes for the thousands served by BHS. I will be depending on your help in this project.

Walef Jones

Figure. Sample letters from Dale Jones.

since knowing him I have become a much better correspondent. Often after an issue of *Baylor University Medical Center Proceedings* was published, a handwritten note from Dale Jones would arrive a few days later. Two typical ones are reproduced in the Figure. I will miss his notes.

William C Roberts

—William Clifford Roberts, MD
November 29, 2004

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